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Cover: Electron micrograph of a sperm cell fertilizing an ovum. (courtesy David M. Phillips, The Population Council).

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Mustard Gas, Bees and DNA

Matthew Meselson Speaks on the Political, Military and Ethical Issues of Biology

by Michael Charles Edwards

Matthew Meselson, Thomas Dudley Cabot Professor of the Natural Sciences and Professor of Biochemistry and Molecular Biology at Harvard University, visited Yale as part of the Johnathan Edwards College Tetelman Fellowship Lecture series.

Dr. Meselson received international recognition as a graduate student at the California Institute of Technology in 1957 when he and Franklin Stahl conducted an experiment that demonstrated semi-conservative replication of DNA. He was also responsible for the invention of ultracentrifugal gradient density analysis of DNA which has been an essential tool in advances in genetic research the past three decades.

During the 1960's, Meselson was an important consultant to the Arms Control and Disarmament Agency and he played a key role in Richard Nixon's decision to unilaterally destroy the U.S. stockpile of biological weapons and to renounce biological warfare. Recently, Meselson received national attention when he and other researchers challenged claims by the Reagan Administration that Soviet-supported Vietnamese and Laotian troops were using mycotoxins against Hmong villagers. His research team including former Yale professor Thomas Seeley showed that the "yellow rain" was actually the excrement of indigenous honeybees.

Meselson is currently doing research in molecular genetics.

YSM: To what extent do you think that the current stockpile of Chemical and Biological Weapons (CBWs) and their potential use threaten the ecosystem?

Michael Edwards is a freshman in Trumbull.

Meselson: Not very much. First of all, there are no confirmed stocks of biological weapons. Chemical weapons, yes; there are substantial stocks of nerve gas and mustard gas which could cause local damage to the environment near a battlefield--but probably less damage than would be inflicted by high intensity use of explosives. I do not think that herbicides will ever be used again in war. They were a flop in Vietnam. They probably imposed more military costs on the U.S. forces than any benefits they produced. We have renounced their use.

YSM: Have inroads been made to apply biological research to biological weapons?

Meselson: That was going on up until 1969. We had a program and we were stockpiling biological weapons. But President Nixon ordered this program stopped and all these weapons to be destroyed. This U.S. policy was unilateral without any *quid pro quo*. Then, a little more than a year later, an international treaty came into force which prohibits the possession of biological weapons.

YSM: Where is your concern for chemical and biological weapons focused?

Meselson: My concern focuses on making sure that the current policy of the United States is maintained because it is a good policy. Also, I am concerned with helping to make sure that our intelligence estimates of what other countries are doing are made with the best possible scientific advice. It is also important that the public not be misled by claims sometimes seen in the newspapers that a new age of biological weapons is dawning. I think this is nonsense and can have only a mischievous effect.

YSM: Given that the Soviet Union is a closed society and the United States is relatively open, how does one verify compliance with such biological weapons treaties?

Meselson: Their society is relatively closed but not completely. They are exactly as open as we are from the sky. The transmission coefficient of air is the same whether that air is over the Soviet Union, the U.S., or any other place. And, of course, satellite reconnaissance and high altitude aircraft reconnaissance are immense enterprises these days. Their resolution is impressive. We know a great deal about what exists in the Soviet Union and they know a great deal about what exists here. And we know a great deal about changes--the same way an astronomer sees changes in the stars by comparing last night's photo with last year's photo.

YSM: Could you talk a little about the Aspen Study Group that investigated CBWs in Europe?

Meselson: We had a meeting in Berlin. There were people with different viewpoints, a retired general and people from various NATO countries. It was a NATO orientated meeting. The question at issue was the role of chemical weapons in NATO's military posture. The final report was mainly an attempt to summarize the different viewpoints. It concluded that the military utility of chemical weapons was, first of all, subject to doubt. In many cases that you can point to today, chemical weapons would be quite a bit less effective than improved high explosive weapons.

Although this was not something that we discussed in Aspen in any intense sense, a good example to consider is the Iran-Iraq War. We have the

If gas is a devastating battlefield weapon, why aren't the Iraqis doing any better...?

spectacle of the one sided use over a period of years of a quite effective chemical agent, namely mustard gas, by only the Iraqis. Yet the Iraqis are the ones winning this war; they are sitting on Iraqi real estate. They have the initiative militarily, but they have not seen fit to use any gas. Now, if gas is a devastating battlefield weapon, why aren't the Iraqis doing any better and why aren't the Iraqis retaliating with gas? The defenses against gas were good even in World War I, and they have been greatly improved. The gas mask today is a far more convenient thing to wear than the old ones. I think gas is overrated. The time that it is effective is

when you can throw a body of men into panic. However, this is largely a question of morale or discipline.

YSM: So if the utility of these CBWs as proven by the Aspen Study Group and historical analysis is minimal, what is the role of these weapons?



Meselson: We concluded that there might occur special situations of a limited nature where it would have some military utility. Although it would never be in NATO's interest to initiate it, there is an argument that can be made for having a limited stockpile for deterrence and for possible reprisal in kind. We agreed that the logical place for this stockpile is in Europe. So we took a pretty dim view of the decision of the President to remove the limited stockpiles from Germany. Their current supply, in my opinion, is enough for two weeks of pretty intensive gas artillery warfare.

Finally, we noted there is an immense down side risk. Soldiers have gas masks but not civilians. You could imagine a brief gas war in Europe killing several million civilians. This is not only horrible to contemplate but the escalatory political impact is immense because the casualty rates would be comparable with nuclear war.

YSM: Would, therefore, the best solution to the aggressive use of CBWs be their elimination, realizing that their use harms both sides?

Meselson: I think that everyone would agree that if you could verifiably get rid of chemical weapons, this would be the best solution. Military people generally do not like chemical weapons--some chemical corps

people do. Many outstanding commanders have felt that chemicals would be a waste of time. The United States, the Soviet Union and thirty-eight other nations have been negotiating a chemical weapons treaty at Geneva since 1977. Although the progress has been slow, they have gotten closer and closer to agreement.

They agree that there should be a treaty completely banning chemical weapons and that it should be verified by international on-site inspection. All the parties to the treaty would declare their inventory of chemical weapons

You could imagine a brief gas war in Europe killing several million civilians.

and their production facilities. Then, all of this should be destroyed within ten years. The destruction of the weapons and the facilities of production would also be verified by on-site international inspection. The Soviets agree that we could inspect their weapons at the site designated for their destruction but we could not monitor them until they reach the destruction site. We, however, want to be able to go and look at the weapons within thirty days of the treaty coming into force--wherever they are located. The difference might be resolved by moving the weapons to the destruction sites before the treaty comes into force.

There is also disagreement regarding the procedure for challenge inspections. Over the years, there has been very substantial progress. Chemical warfare treaties with the degree of inspection necessary for verification are possible without being so intrusive as to be really useful for espionage.

YSM: What were the circumstances surrounding your research on "yellow rain" and what was the response of the Reagan Administration?

Meselson: I had been a consultant to the various parts of the government on chemical warfare matters from 1963 until 1981. I was asked to come into the intelligence community and receive a briefing on the yellow rain. Before that date arrived, they called back and said that the plan was not operational. So I was never involved in the official assessment of the yellow rain.

Then, in November 1982, the State Department published an on-the-record briefing saying that most of the samples of yellow rain were dry and mainly composed of pollen. It was not the kind of pollen that was wind borne but the kind of pollen that would be gathered by insects. They went beyond that and said it was the kind of pollen that would be gathered by honey bees.

They were the first to say anything about bees. They

went on to say why they thought the Soviets would mix this kind of pollen with chemical warfare agents. Their explanation was that the material as it falls is wet but that when it dries up, the wind would disperse the pollen grains in which toxin has been introduced. These particles would be of such a small size as to penetrate into the deep recesses of the lungs. When I read that, I knew their investigations were in rather bad shape. First of all, it seemed rather loony that the Russians would go around collecting pollen from bee nests. Moreover, it is not possible for wind to convert a congealed deposit of a few millimeters in diameter into individual micron-sized particles. So, I knew that it was utter nonsense and the fact that they would not only be entertaining this hypothesis, but would actually publish it, meant that they were lost. Furthermore, they had been receiving samples of yellow rain beginning in the middle of 1979. Why had they not discovered that there was pollen in it until 1982? It was because they had not looked at it under the microscope. Because they were expecting to find poisonous compounds, they used methods of molecular analysis, not morphological analysis.

The first people who did recognize the pollen were at the British military chemical defense laboratory. This led to a long series of investigations of the pollen in yellow rain samples by Joan Nowicke of the Smithsonian Institute. Tom Seeley came up with the correct idea that it was bee dropping. We did many things to analyze this hypothesis and in every respect we tested, it proved right. But officially, the United States government still supports their original claim.

The plain fact is that senior scientists in the intelligence community privately agree that the yellow rain is bee feces. But government policy just cannot be changed when government scientists see that it is wrong. The policy can only be changed by an event called an inter-agency review which brings together the representatives of the different agencies. They sit down and review, and then they come up with a finding, which goes all the way up to the President, in this case because the President himself

It seemed rather loony that the Russians would go around collecting pollen from bee nests.

has asserted on many occasions both verbally and in writing that the yellow rain is mycotoxin warfare. To my knowledge, nobody in authority has requested an inter-agency review. There is not a big incentive to prove that their previous assessment was wrong. So, you have this odd situation where they know it's wrong and yet it remains government policy.

YSM: I would like to discuss your very famous work on DNA replication. When Watson and Crick first elucidated the structure of DNA, what was the mood of the scientific community? Were you involved in this great race to discover the structure?

Meselson: No, I certainly was not. I was a

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graduate student of Linus Pauling at Caltech at the time, working on the structure of a small peptide. I did not even know about the publication of the structure of DNA when it came out in April of 1953. It was at least a few weeks later when I went to meet Max Delbruck. He was the leading molecular biologist at Caltech. He had a fearsome reputation. I went to introduce myself and at Caltech things are pretty informal. He asked me what I thought about Watson and Crick's papers in *Nature*. I said I had not heard of them. He had a little stack of them on a shelf behind his head and he threw them at me as he said, "The most important discovery in biology in the decade and you have not even heard of it. Don't come back and see me until you've read these papers." I did not think that was fearsome at all. I thought that was pretty good because he was saying he wanted to talk with me again. Then I read the papers and it took me a long time before I understood the X-ray crystallographic arguments. But, I was not part of that scene initially. I had to finish my thesis work in X-ray crystallography. Then while I was still a graduate student, Frank Stahl and I did the experiment on how DNA replicates. We are still working on some aspects of these things.

YSM: With this history of seeing biological advances, you have a certain perspective of current research. What areas today in modern biology do you see as the key to future advances?

Meselson: Over the longer term, I think human beings will start guiding their genetic destiny by changing their germ lines and thereby directly intervening in the evolutionary process. In mice you can inject DNA into the germ cells and some of the DNA molecules will be taken up and will be expressed. You cannot introduce them just where you want and you cannot replace existing genes with new genes. This can be done in bacteria and yeast. But all of the

technical wrinkles will be overcome, and it will be possible to substitute new genes for old genes in the germ line and to put in genes that have no counterpart at present. What if there was a gene whose product meant that you could not have neoplastic disease? Today, parents favor the inoculation of their children



against various infectious diseases. What if you could put a gene in the germ line which meant there would be no more cancer in that person or in any of his descendants who inherited that allele? Initially, no parents would want to because there would be religious and ethical barriers. But once it gets going, then it's much more difficult to say no. That will raise the question what is it to be human. What are the best features of being human? That is a good question for people to be thinking about.